510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k060574

B. Purpose for Submission:
Clearance of a new device

C. Measurand:
Bilirubin, Total

D. Type of Test:
Quantitative Absorbance Assay

E. Applicant:
Abbott Laboratories

F. Proprietary and Established Names:
Total Bilirubin for the AEROSET System and the ARCHITECT *c8000* System.

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1110, Bilirubin (total or direct) test system
   21 CFR § 862.1150, Calibrator

2. Classification:
   Class II

3. Product code:
   CIG, Diazo colorimetry, bilirubin;
   JIT, Calibrator

4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   The Total Bilirubin assay is used for the quantitative analysis of total bilirubin in human serum or plasma of adults and neonates.

2. Indication(s) for use:
   The Total Bilirubin assay is used for the quantitation of total bilirubin in human serum or plasma. Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the

diagnosis and treatment of liver, hemolytic hematological, and metabolic disorders, including hepatitis and gall bladder block.
A bilirubin (total and unbound) in the neonate test system is a device intended to measure the levels of bilirubin (total and unbound) in the blood (serum) of newborn infants to aid in indicating the risk of bilirubin encephalopathy (kernicterus).

3. Special conditions for use statement(s):
   For prescription use

4. Special instrument requirements:
   The AEROSET System or the ARCHITECT *c8000* System.

I. Device Description:

Total Bilirubin is an in vitro diagnostic assay for the quantitative determination of total bilirubin in human serum or plasma of adults and neonates. Total (conjugated and unconjugated) bilirubin couples with the diazo reagent in the presence of a surfactant to form azobilirubin. The increase in absorbance at 548 nm due to azobilirubin formation is directly proportional to the total bilirubin concentration. The assay is supplied as a liquid, ready to use, two reagent kit. The calibrator materials are sold separately and are prepared in bovine serum-based solution. The analyte concentrations for the calibrators are adjusted using bilirubin extracts and synthetic derivatives.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche Total Bilirubin assay on the Hitachi 717 Analyzer

2. Predicate 510(k) number(s):
   k910591

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Total Bilirubin assay is used for the quantitative analysis of total bilirubin in human serum or plasma of adults and neonates.	The Total Bilirubin assay is used for the quantitative analysis of total bilirubin in human serum or plasma of adults and neonates.
Detection	Absorbance	Absorbance
Sample Types	Plasma and Serum	Plasma and Serum
For Use In	Adults and Neonates	Adults and Neonates

Similarities		
Item	Device	Predicate
Test Method	Coupling with the diazo reagent in the presence of a surfactant to form azobilirubin and detection at 548 nm.	Coupling with the diazo reagent in the presence of a surfactant to form azobilirubin and detection at 548 nm.

Differences		
Item	Device	Predicate
Assay Range	0.1-25.0 mg/dL	0.1-35.0 mg/dL
Reference Ranges	Premature Newborn (mg/mL): <24 hours <8.0 <48 hours <12.0 3 to 5 days <15.0 7 days <15.0 Full Term Newborn (mg/mL): <24 hours <6.0 <48 hours <10.0 3 to 5 days <12.0 7 days <10.0 Adult: 0.2-1.2 mg/dL	Premature Newborn (mg/mL): 24 hours 1.0-6.0 48 hours 6.0-8.0 3 to 5 days 10.0-15.0 Full Term Newborn (mg/mL): <24 hours 2.0-6.0 <48 hours 6.0-7.0 3 to 5 days 4.0-12.0 Adult and Children: Up to 1.0 mg/dL
Instrument Required	The AEROSET System or the ARCHITECT *c8000* System.	Hitachi 717 Analyzer

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods
CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach
CLSI EP9-A2, Evaluation of Precision Performance of Quantitative Measurement Methods
CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation

L. Test Principle:

See Device Description above.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

   Four control levels (Level 1, Level 2, Level 3, and Level 4) at normal and abnormal analyte concentrations were tested. These controls were evaluated

over 20 days, two runs per day, and two replicates per run. The sponsor considered the precision acceptable if the total %CV is ≤5%. Two patient serum pools and three control materials were assayed. Results for precision are summarized below.

AEROSET Precision

	Control Level 1	Control Level 2	Control Level 3	Control Level 4
N	80	80	80	80
Mean, µIU/mL	0.82	4.16	6.10	16.27
	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)
Within Run	0.01(0.65)	0.02(0.47)	0.02(0.3)	0.01(0.61)
Between Run	0.01(0.71)	0.04(0.92)	0.05(0.76)	0.09(0.54)
Between Day	0.01(0.93)	0.05(1.17)	0.06(1.04)	0.06(0.39)
Total	0.01(1.33)	0.07(1.56)	0.08(1.32)	0.15(0.90)

ARCHITECT *c8000* Precision

	Control Level 1	Control Level 2	Control Level 3	Control Level 4
N	80	80	80	80
Mean, µIU/mL	0.81	4.07	6.03	16.09
	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)
Within Run	0.01(0.97)	0.02(0.49)	0.03(0.55)	0.12(0.74)
Between Run	0.01(0.71)	0.04(0.92)	0.04(0.63)	0.03(0.19)
Between Day	0.01(1.17)	0.08(1.86)	0.1(1.64)	0.17(1.05)
Total	0.01(1.68)	0.09(2.13)	0.11(1.84)	0.21(1.3)

b. Linearity/assay reportable range:

The linear range for the Total Bilirubin assay was determined for both the AEROSET System and the ARCHITECT *c8000* System. Nine samples at various concentrations spanning 0.054 to 27.967 mg/dL over two lots for the AEROSET and 0.042 to 27.913 mg/dL over two lots for the ARCHITECT *c8000* were run in a minimum of four replicates. The percent recovery for each sample was determined by dividing the mean observed result by the

predicted value. The sponsor's acceptable difference between the observed result and the predicted value was within 10% or each replicate was within the 95% confidence interval of the predicted value for each level. Results are summarized below.

AEROSET Linearity

	Level	Mean Conc. (mg/dL)	Predicted Values (mg/dL)	% Difference (Point Estimate)
Lot 1	1	0.054	0.205	-73.93
	2	0.105	0.268	-60.96
	3	0.169	0.330	-48.89
	4	1.759	1.767	-0.504
	5	6.557	6.454	1.588
	6	12.911	12.703	1.637
	7	19.836	18.952	4.665
	8	25.144	25.200	-0.225
	9	27.672	28.325	-2.305
Lot 2	1	0.041	0.152	-73.05
	2	0.095	0.214	-55.71
	3	0.155	0.277	-44.19
	4	1.753	1.711	2.467
	5	6.462	6.387	1.174
	6	12.733	12.621	0.886
	7	19.537	18.856	3.610
	8	24.775	25.091	-1.260
	9	27.967	28.208	-0.853

ARCHITECT *c8000* Linearity

	Level	Mean Conc. (mg/dL)	Predicted Values (mg/dL)	% Difference (Point Estimate)
Lot 1	1	0.042	0.160	-73.51
	2	0.101	0.222	-54.34
	3	0.161	0.284	-43.46
	4	1.751	1.717	1.940
	5	6.499	6.391	1.699
	6	12.622	12.622	0.004
	7	19.508	18.853	3.474
	8	25.319	25.084	0.934
	9	27.530	28.200	-2.377
Lot 2	1	0.046	0.157	-70.89
	2	0.106	0.220	-51.61
	3	0.167	0.283	-40.99

	4	1.764	1.726	2.222
	5	6.525	6.430	1.474
	6	12.713	12.703	0.072
	7	19.654	18.977	3.568
	8	25.245	25.250	-0.020
	9	27.913	28.386	-1.667

Linear regression analysis gave the following:

AEROSET Lot 1: Observed = 0.999(Expected) + 0.0005; r = 0.9993
AEROSET Lot 2: Observed = 0.999(Expected) + 0.0002; r = 0.9997
ARCHITECT c8000 Lot 1: Observed = 0.999(Expected) – 0.0002; r = 0.9995
ARCHITECT c8000 Lot 2: Observed = 0.999(Expected) – 0.00001; r = 0.9996
The reportable range of the assay is 0.1 – 25.0 mg/dL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Internal reference standards are manufactured by gravimetric methods and are traceable to NIST SRM 916a. The internal reference standards are used for the determination of calibrator value assignments at each level. Calibration is stable for 14 days (336 hours) for this assay.

d. *Detection limit:*

The Limit of Quantitation (LoQ) (the analytical concentration at which the pooled analyte "within instrument" CV = 20%) was determined by measuring 20 spiked samples on 3 instruments for two lots for both the AEROSET System and the ARCHITECT *c8000* System. Concentrations ranged form 0.0767 to 0.0893 mg/dL over two lots for the AEROSET and 0.0795 to 0.0913 mg/dL over two lots for the ARCHITECT *c8000*. The data submitted supports a LoQ of 0.1 mg/dL.

The Limit of Detection (LoD) (the lowest amount of analyte in a sample that can be detected with 95% probability) was determined by measuring 20 samples on 3 instruments for two lots for both the AEROSET System and the ARCHITECT *c8000* System. The data submitted supports a LoD of 0.02 mg/dL. The sponsor will claim a higher LoD of 0.05 mg/dL in the labeling.

e. *Analytical specificity:*

Solutions of human serum albumin were spiked with bilirubin to create two levels of bilirubin. The two solutions were spiked with various levels of interferants. A minimum of seven replicates of each interferant level and seven replicates of reference samples were run. The percent recovery was

determined by dividing the mean result of the replicates for each interferant level by the mean result of the replicates for the reference sample. The sponsors acceptance criteria was set at +/- 10% or +/- 0.3 mg/dL difference between the interferant results and the reference result, whichever is greater.

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed	
			(mg/dL)	(% Target)
Indican	0.031 mmol/L	1.146	1.318	115.01
	0.062 mmol/L	1.146	1.507	131.53
	0.25 mmol/L	18.207	19.603	107.67
	0.5 mmol/L	18.207	21.020	115.45
Hemoglobin	1000 mg/dL	1.062	0.918	86.39
	2000 mg/dL	1.062	0.854	80.36
	1000 mg/dL	16.411	15.733	95.87
	2000 mg/dL	16.411	15.533	94.65
Intralipid	1000 mg/dL	1.033	1.188	115.02
	2000 mg/dL	1.033	1.403	135.80
	1000 mg/dL	16.632	16.634	100.02
	2000 mg/dL	16.632	16.824	101.16

f. Assay cut-off:
Not Applicable (NA)

2. Comparison studies:

a. Method comparison with predicate device:

One hundred thirty-seven adult samples and 52 neonate samples (minimum of one replicate per run) were tested using each method. A total of 24 adult samples were spiked with a Bilirubin NIST SRM916a Standard (100 mg/dL) to generate high analytical levels. A linear regression analysis was performed comparing results for each method. Results are summarized below.

Method Comparison for Adults

	AEROSET vs. Hitachi	ARCHITECT vs. Hitachi	AEROSET vs. ARCHITECT
N	137	137	137
y – intercept	0.22	0.20	-0.02
Correlation Coefficient	0.9992	0.9992	0.9999
Slope	0.96	0.95	0.99
Range (mg/dL)	0.21 to 24.41	0.21 to 24.41	0.27 to 22.77

Method Comparison for Neonates

	AEROSET vs. Hitachi	ARCHITECT vs. Hitachi	AEROSET vs. ARCHITECT
N	52	52	52
y – intercept	0.22	0.06	-0.13
Correlation Coefficient	0.9934	0.9921	0.9964
Slope	0.96	0.98	1.02
Range (mg/dL)	4.65 to 15.9	4.65 to 15.9	4.80 to 15.79

b. Matrix comparison:

Ten subjects were used to compare total bilirubin results of a glass baseline serum tube (with Bilirubin levels ranging from 0.257 to 0.895 mg/mL) to plastic sodium heparin, lithium heparin with and without gel barrier, EDTA and plastic tubes. The sponsor's acceptance criteria were set at +/- 10% or +/- 0.2 mg/dL difference between the interferant result and the reference result, whichever is greater, between the mean values of each sample for each tube type in question and the plain glass serum tube. The data submitted demonstrates an acceptable difference from the glass tube serum baseline on both the AEROSET and the ARCHITECT *c8000* Systems.

3. Clinical studies:

a. Clinical Sensitivity:
NA

b. Clinical specificity:
NA

c. Other clinical supportive data (when a. and b. are not applicable):
NA

4. Clinical cut-off:
NA

5. Expected values/Reference range:

Serum samples from 135 apparently healthy adult blood bank donors (ages 25 to 66) were commercially purchased and assayed with the previously cleared Abbott Total Bilirubin assay (k022339). The expected normal range for this assay was found to be 0.2 to 1.2 mg/dL based on the central 95% of the frequency of distribution. A confirmation study was conducted using 25 serum and plasma

samples from adult volunteers using the submitted device. All specimens tested fell within the range of 0.2 to 0.9 mg/dL.

The neonate reference ranges are referenced from:
Jacobs DS, Oxley DK, editors. *Laboratory Test Handbook*, 5th ed. Hudson, OH: Lexi-Comp; 2001:117-8.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.